

Molecular Mechanisms of Trophoblast Stem Cell Specification and Self-Renewal

Grant Award Details

Molecular Mechanisms of Trophoblast Stem Cell Specification and Self-Renewal

Grant Type: New Faculty II

Grant Number: RN2-00931

Project Objective: The goal of this project is to gain better understanding of the molecular mechanisms that control the fate of various placental cell types in humans.

Investigator:

Name: Mana Parast

Institution: University of California, San Diego

Type: PI

Disease Focus: Fertility

Human Stem Cell Use: Adult Stem Cell, Embryonic Stem Cell

Award Value: \$3,077,918

Status: Closed

Progress Reports

Reporting Period: Year 1

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Grant Application Details

Application Title:	Molecular Mechanisms of Trophoblast Stem Cell Specification and Self-Renewal
Public Abstract:	<p>Prematurity/preterm birth is the leading cause of neonatal death in the U.S. and in California. During an average day in California, 149 babies are born preterm. These babies are at increased risk for long-term disabilities, including cerebral palsy, gastrointestinal problems, and vision and hearing loss. Many premature babies also suffer from low birth weight, which not only increases complications in the perinatal period, but also leads to increased cardiovascular disease and diabetes in adulthood. Finally, prematurity and fetal growth restriction are many times the result of obstetric diseases, such as pregnancy-induced hypertension and seizures, which carry high rates of maternal morbidity and mortality. All the above-mentioned diseases result from abnormal development and function of the placenta, which is a transient organ that forms the interface between mother and baby. Trophoblasts are the primary cell type which carries out major placental functions such as establishing blood supply from the mother to the fetus. This application proposes the placenta as a novel target for stem cell therapy and seeks generation of trophoblast stem (TS) cells, which give rise to all subtypes of trophoblasts in the placenta. This research will lead to identification of specific trophoblast markers, which can then be developed into diagnostic tools to use in prenatal screening for placental function and fetal well-being. Most importantly, it will lead to development of trophoblast stem cell-based therapeutics for in-utero intervention in cases of fetal growth restriction, preterm labor, and pre-eclampsia. Prevention of these complications will substantially decrease both neonatal and maternal morbidity and mortality; in addition, treatment of growth restriction in the fetus will in turn decrease cardiovascular disease and diabetes in later life. Thus funding this grant would be a small investment towards substantially improving the health of future generations and alleviating the financial burden caused by premature birth and its complications in California.</p>

Statement of Benefit to California:

The goal of every pregnant mother is to have a healthy baby. Unfortunately, pregnancy can be complicated by many diseases, which affect the placenta, the lifeline of the baby. When the placenta develops abnormally or malfunctions, babies are born small and/or premature. This leads to many complications in the perinatal period, including bleeding and abnormal development of the brain, blindness, and gastrointestinal problems. These complications usually require long stays in neonatal intensive care units, with an average per patient cost of over \$20,000, compared to \$1,300 for a normal weight term baby in the regular newborn nursery. Even when the small premature baby survives the neonatal period, s/he will face an increased risk of complications as a teenager and later an adult, including cardiovascular disease and diabetes, adding to the already over-burdened healthcare system. But what if we could prevent all these problems before they started, in utero, by treating the placenta? The research proposed in this application could make that possibility a reality, by developing trophoblast stem cells. There is very little known about trophoblast stem cells, because the majority of stem cell research today is focused on embryonic stem cells that become the embryo and give rise to adult organs, like the brain, heart, and pancreas. Virtually nothing is known about the "other" stem cells in the human blastocyst, the trophoblast shell that becomes the placenta. This research would start a whole new direction in the field of stem cell research. It would lead to a greater understanding of placental development and diseases, which many mothers and babies face every day. But most importantly, it would benefit the state of California by leading to therapies aimed at preventing pre-term birth and fetal growth restriction. This will not only improve the health of the future generation of Californians, it would save the state over \$200 million annually in neonatal care. Aside from direct contributions towards improving the health of California's population, funding this grant will contribute to jump-starting careers of not just one, but two physician-scientists, which are extremely rare in the field of perinatal medicine, not just in California, but world-wide. Funding this grant would greatly contribute to the development of two leaders in this field and, through their interactions with other physicians-in-training, lead to attraction of more trainees to research careers in perinatal medicine.

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